REMARKS

Applicants respectfully request reconsideration and allowance of the claims, as amended, in light of the remarks made herein. The Examiner is thanked for indicating that claim 3 is allowable.

Claims 3, 5-8, 11-23 and 27-33 are under examination in this application. Support for each amendment can be found throughout the specification and from the claims as filed. Most of the amendments have been made simply to address formal matters, to correct dependence, and to place the claims in condition for allowance, or at least in better condition for appeal. No new matter has been added.

All of the claims relate to the antibacterial Salivaricin B protein. Independent claim 3 and dependent claims 5 and 6 are each directed to a protein. Claims 7 and 8 (both dependent) are directed to a composition and therapeutic formulation, respectively, comprising the protein of claim 3. Claims 10-23 are all dependent claims directed to therapeutic formulations. Claims 27-31 are directed to microorganisms. The microorganisms of claims 30 and 31 are bacterial strains that produce Salivaricin B endogenously; the microorganism of claims 27-29 comprises the protein of claim 3. Dependent claim 32 is directed to a therapeutic composition comprising the microorganism of claim 30 or 31. Claim 33 is a method of treatment claim involving administering the protein of claim 1 to an individual. Therefore, claims 3, 30 and 31 are the only independent claims pending in this application.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art, and that these claims are and were in full compliance with the requirements of 35 U.S.C. §112. The amendments of and additions to the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendments should not give rise to any estoppel, as the herewith amendments are not narrowing amendments.

The Rejections Under §112 Are Overcome

Claims 1, 2, 4-23 and 27-40 were rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. As was raised in the Amendment filed on March 14, 2003, this rejection is once again presented as an enablement rejection, yet is discussed in terms of what the

Applicants possessed, as would apply for a written description rejection. The Office Action states on the top of page 3 that "[t]he rejection is under 35 U.S.C. 112, first paragraph"; however, as was reaffirmed in 1991 by the Federal Circuit in *Vas-Cath, Inc. v. Mahurkar* (935 F.2d 1555,1562, 19 USPQ2d 1111, 1115), the written description requirement is separate and distinct from the enablement requirement. Therefore, Applicants will point out why both written description and enablement exist for the pending claims.

The Office Action contends that "[t]here is no evidence on the record that applicant was in clear possession of a protein other than SEQ ID NO:3." While this is untrue, the claims have been limited to the protein of SEQ ID NO:3, of which the Examiner has admitted Applicants have possession, in order to expedite prosecution of this application. It should be noted, however, that the Declaration of Dr. John Tagg, submitted with the March 14, 2003 Amendment ("the first Tagg Declaration"), describes a variant of the Salivaricin B protein, isolated from *Streptococcus mitis*. This protein has a histidine, rather than an arginine at position 13, and yet has substantially the same activity profile as the protein of SEQ ID NO:3, as shown in Exhibit 2 of the Declaration. Therefore, Applicants are "in clear possession of a protein other than SEQ ID NO:3", contrary to the statement in the Office Action.

With respect to enablement, according to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988):

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. **The key word is undue, not experimentation.** The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Emphasis added. Citations omitted].

Id. at 1404.

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing many factors summarized in *In re Wands* (*Id.*), for example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the

nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims.

Applying *Wands* to the instant facts, enablement is shown to exist. The amount of direction or guidance presented is high; working examples are present; the synthesis of polypeptides and the determination of antibacterial activity is routine; the relative skill of those in the art is high; and the predictability of the art is also high. No evidence to the contrary has been presented. The skilled artisan would face no undue experimentation in isolating or synthesizing a protein having the amino acid of SEQ ID NO:3, or in making a composition or formulation comprising said protein. Therefore, claims 3 and 5-23 are clearly enabled by the application. Likewise, because the protein of claim 3 is enabled by the application, there is no reason that a microorganism comprising the protein is not enabled. In fact, the inventors have provided two such organisms, strains, K12 and K30, and have deposited them under the provisions of the Budapest Treaty.

Furthermore, it should be noted that neither the non-final Office Action of November 14, 2002, nor the final Office Action of June 3, 2003 makes any rejection under the first paragraph of Section 112 that is based on the microorganism aspect of the invention. Rather, the rejections focus on which proteins are or are not allegedly enabled. (See first paragraph on page 3 of the November 14, 2002 Office Action and first paragraph on page 3 of the June 3, 2003 Office Action.) It should also be noted that the amendment to claim 27 removes, rather than adds, subject matter, and that the amendments to claims 28 and 29 address a minor formality. Otherwise, claims 27-32 are presented basically as originally filed. Therefore, any rejection of claims 27-32 under 35 U.S.C. §112 would be a NEW rejection, and improper in view of the after-final status of the application.

The same line of reasoning also applies to claim 33, as there was never, in the entire prosecution history, a written description or enablement rejection that challenged the method of treatment claims. Rather, all rejections of claim 33 were based upon its dependence on claims that recited variants of SEQ ID NO:3. Further, the only amendment that has been made to claim 33 is the current one, to remove the dependency on cancelled claims. Therefore, like claims 27-32, claim 33 also cannot properly be rejected under 35 U.S.C. §112 at this point in prosecution, unless a new, non-final Office Action is issued.

Claims 1, 5-23, 27-29 and 33-39 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Claim 1 has been cancelled, obviating its rejection and the rejection of its dependent claims, 5-23, 27-29 and 33-39.

In addition, several amendments were made to address improper multiple dependence (claims 11, 14, 15, 19 and 21) and antecedent basis (claims 12-14). Although the claims were not rejected on these bases, such amendments place the claims in better form.

In view of these arguments and amendments, the claims are in compliance with 35 U.S.C. §112; and reconsideration and withdrawal of all of the rejections thereunder are requested.

The Rejections Under 35 U.S.C. §102 and §103 Are Overcome

Claims 1, 2, 4-15, 21-23 and 27-40 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Caufield *et al.* Claims 1, 2, 4-23 and 27-40 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Caufield *et al.* These rejections are moot, given the fact that none of the cited references teach or suggest a protein having the amino acid sequence of SEQ ID NO:3, and can therefore not anticipate any of claims 3, 5-23, 27-29 or 33. Moreover, claims 30-32 are directed to specific strains of *S. salivarius* that were isolated for the first time by the current inventors, as attested to by the attached Declaration under 37 CFR 1.132 by inventor Dr. John Tagg ("the second Tagg Declaration"). These strains are clearly novel, and the Examiner has not presented any evidence to the contrary.

It should be noted that Caufield *et al.* relates to a protein isolated from *Streptococcus mutans*. Regardless of the difference or similarity of the Caufield sequence to SEQ ID NO:3 (which is discussed in detail below), it is unclear why claims 1 and 29-32 were included in these rejections, as they specifically recite *Streptococcus salivarius*. If this rejection is maintained, it is respectfully requested that the Examiner clarify his reasoning with respect to the inclusion of claims 1 and 29-32 in this rejection.

The Office Action of November 14, 2003 identified the Caufield reference as publishing a sequence that is a 86.9% match to SEQ ID NO:3. While the sequence similarity between SEQ ID NO:3 and Caufield is a moot point, give the fact that the claims have been limited to SEQ ID NO:3, Applicants present the following argumentation to have the record reflect the true relationship between SEQ ID NO:3 and that of Caufield. Once again, Applicants point out that the match is actually 84%, as is shown in the "best local similarity" field of the computer readout

presented with the Office Action. Applicant have not "decided to create their own system or algorithm", as is alleged in the Office Action. Rather, Applicants have simply performed straightforward arithmetical calculations: twenty-one of the twenty-five amino acid residues in SEQ ID NO:3 are identical to the sequence of Caufield, as is shown in the computer readout.

$$21/25 \times 100 = 84\%$$

Regardless, the pending claims are directed to the protein of SEQ ID NO:3, compositions, formulations, and organisms comprising said protein, and a method of treatment comprising administering said protein, none of which are taught or suggested by Caufield.

Claims 1, 2, 4-23 and 27-40 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Ross *et al.*, Tagg, Sanders *et al.*, Matsushiro or Kawai *et al.* Claims 1, 2, 4-23 and 27-40 were also rejected under 35 U.S.C. §103(a) as allegedly obvious over Ross *et al.*, Tagg, Sanders *et al.*, Matsushiro or Kawai *et al.* taken with Caufield *et al.* These rejections are moot with respect to claims 3 and dependent claims 5-23, in view of the fact that claim 3 was not included in this rejection.

There are several flaws in these rejections. Firstly, it is noted that claim 1 was directed to a protein isolated from strain K12 of *S. salivarius*, and claims 29-32 are directed to cultures of *S. salivarius* strain K12 or K30, therapeutic formulations comprising said cultures, and the organisms themselves. These strains were first identified by the inventors of the instant application, as is confirmed in the second Tagg Declaration. Not one of the cited references teaches, discusses, or even suggests strains K12 or K30 or any proteins isolated from them, because these strains were **unknown** before being identified by Dr. Tagg and his coworkers. Therefore, no reasonable case has been or could be presented as to why Ross *et al.*, Tagg, Sanders *et al.*, Matsushiro or Kawai *et al.*, alone or in any combination, anticipate or render obvious the subject matter of any of claims 1 or 29-32.

Secondly, none of the references relied upon by the Examiner teach or suggest an isolated antibacterial protein having the sequence of SEQ ID NO:3. So even if, as the Examiner argues, the claimed protein is inherent to the microorganisms discussed in the cited references, and Applicants do not admit that they are, an anticipation rejection is improper with respect to claim 3, and claims dependent thereon (i.e. claims 5-23), because these claims are limited to an isolated protein. The isolated protein, as claimed, is not described or suggested in any of the references cited by the Examiner.

Addressing the inherency aspect of the anticipation rejection with respect to Ross *et al.*, Tagg, Sanders *et al.*, Matsushiro and Kawai *et al.*, the Office Action alleges, on page 4, that "[t]he same microorganism is used thus the same protein is obtained." This statement is incorrect. The organisms described in the instant application are *S. salivarius* strains K12 and K30. Ross relates to *S. salivarius* strain 20P3; Sanders relates to *S. salivarius* strain K58; Matsushiro relates to *S. salivarius* strains M-33 and G8326; and Kawai relates to *S. salivarius* strain ADV10001. The only specific *S. salivarius* strain mentioned in Tagg is Min5. Thus, the same microorganisms are not used in the instant application as in the cited references. And, as is shown in Table 1 of the Tagg reference (cited by the Examiner), and as is emphasized in the first Tagg Declaration, only a small percentage of *S. salivarius* strains tested have been found to produce the claimed protein, Salivaricin B. The Examiner seems to have overlooked the expert declaration in favor of his own opinions.

Furthermore, to establish inherency, the evidence "must make it clear that the missing descriptive matter is **necessarily** present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. **Inherency, however, may not be established by probabilities or possibilities.** The mere fact that a certain thing **may** result from a given set of circumstances is not sufficient." *In re Robertson* 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (emphasis added). *See also* MPEP §2112. There is no evidence to suggest that Salivaricin B is necessarily present in the *S. salivarius* strains mentioned in Ross *et al.*, Tagg, Sanders *et al.*, Matsushiro, Kawai *et al.*, nor is there any reason to believe that, were it present, it would be so recognized by persons of ordinary skill in the art. Therefore, the Examiner has not met the standard prescribed by *In re Robertson* for a rejection based on inherency.

With respect to the obviousness rejection, it is neither taught nor suggested by any of the documents in question that Salivaricin B is produced by any of these organisms. None of the citations teach the production of the protein of the invention, nor has the Examiner established that there would have been any motivation for a person of ordinary skill to make the claimed proteins or variants as presently claimed. There is simply no reason to do so without an appreciation that this 25 amino acid protein is active in its own right, and has distinct bacteriocidal properties.

In view of these arguments, reconsideration and withdrawal of the rejections under 35 U.S.C. §§102 and 103 are requested.

CONCLUSION

Applicants believe that the application is in condition for allowance, and favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. Alternatively, consideration and entry of this paper is requested, as it places this application into better condition for purposes of appeal.

It is believed that no fee is required for the instant submission. However, if any fee is required, or if any overpayment has been made, please charge or credit Deposit Account No. 50-0320.

Respectfully submitted,

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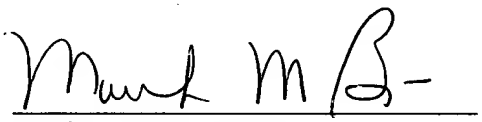
By: 

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